Serial No.: 09/910,639 Filed: July 20, 2001

Page : 2 of 12

Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

1. - 17. (Cancelled)

- 18. (Currently amended) A method of delivering a radiolabeled immunotoxin to a subject suspected of having a cancer, the method comprising:
 - (a) identifying a subject suspected of having a cancer; and
- (b) administering to the subject a radiolabeled immunotoxin comprising a toxic domain, a targeting domain, and at least one radionuclide atom,

wherein the targeting domain is a sFv antibody fragment that binds to a target molecule on a cancer cell in the subject, the target molecule being selected from the group consisting of Her-2/neu, a mucin molecule, CEA, PSA, folate binding receptor, A33 alpha fetoprotein, CA-125 glycoprotein, colon-specific antigen p, ferritin, p-glycoprotein, G250, OA3, PEM glycoprotein, L6 antigen, 19-9, P97, placental alkaline phosphatase, 7E11-C5, 17-1A, TAG-72, 40 kDa glycoprotein, URO-8, a tyrosinase, an interleukin- (IL-)2 receptor polypeptide, an IL-3 receptor polypeptide, an IL-13 receptor polypeptide, an IL-4 receptor polypeptide, a VEGF receptor, a GM-CSF receptor polypeptide, an EGF receptor polypeptide, an insulin receptor polypeptide, an insulin-like growth factor receptor polypeptide, transferrin receptor, estrogen receptor, a T cell receptor (TCR) α -chain, a TCR β -chain, a CD4 polypeptide, a CD8 polypeptide, a CD7 polypeptide, a B cell Ig heavy chain, a B cell Ig light chain, a CD19 polypeptide, a GAGE polypeptide, a RAGE polypeptide, a MAGE polypeptide, and a GnTV polypeptide, and

wherein the at least one radionuclide atom is selected from the group consisting of ⁹⁰Y, ¹⁸⁶Re, ¹⁸⁸Re, ⁶⁴Cu, ⁶⁷Cu, ²¹²Pb, ²¹²Bi, ²¹³Bi, ¹²³I, ¹³¹I, ²¹¹At, ¹⁷⁷Lu, ⁴⁷Sc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹⁵³Sm, ¹⁹⁹Au,

Serial No.: 09/910,639 Filed : July 20, 2001

Page : 3 of 12

^{99m}Tc, ¹¹¹In, ¹²⁴I, ¹⁸F, ¹¹C, ¹⁹⁸Au, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br, ¹³N, ^{34m}Cl, ³⁸Cl, ^{52m}Mn, ⁵⁵Co, ⁶²Cu, ⁶⁸Ga, ⁷²As, ⁷⁶As, ⁷²Se, ⁷³Se, and ⁷⁵Se.

- 19. (Original) The method of claim 18, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) Pseudomonas exotoxin (PE); (c) bryodin; (d) gelonin; (e) α-sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).
- 20. (Original) The method of claim 18, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.
- 21. (Original) The method of claim 20, wherein the functional fragment comprises amino acids 1-389 of DT.

22. (Cancelled)

- 23. (Previously presented) The method of claim 18, wherein the cancer cell is selected from the group consisting of a neural tissue cancer cell, a melanoma cell, a breast cancer cell, a lung cancer cell, a gastrointestinal cancer cell, an ovarian cancer cell, a testicular cancer cell, a lung cancer cell, a prostate cancer cell, a cervical cancer cell, a bladder cancer cell, a vaginal cancer cell, a liver cancer cell, a renal cancer cell, a bone cancer cell, and a vascular tissue cancer cell.
- 24. (Currently amended) The method of claim [[22]] 18, wherein the target molecule is Her-2/neu.

25. (Cancelled)

Serial No.: 09/910,639 Filed: July 20, 2001 Page: 4 of 12

26. (Previously presented) The method of claim 18, wherein the method is a method of killing a target cell in the subject.

- 27. (Previously presented) The method of claim 26, wherein the at least one radionuclide atom is selected from the group consisting of ⁹⁰Y, ¹⁸⁶Re, ¹⁸⁸Re, ⁶⁴Cu, ⁶⁷Cu, ²¹²Pb, ²¹²Bi, ²¹³Bi, ¹²³I, ¹³¹I, ²¹¹At, ¹⁷⁷Lu, ⁴⁷Sc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹⁵³Sm, and ¹⁹⁹Au.
- 28. (Previously presented) The method of claim 18, wherein the method is an imaging method.
- 29. (Previously presented) The method of claim 28, wherein the at least one radionuclide atom is selected from the group consisting of ¹⁸⁶Re, ¹⁸⁸Re, ⁶⁴Cu, ⁶⁷Cu, ²¹²Bi, ¹²³I, ¹³¹I, ²¹¹At, ¹⁷⁷Lu, ⁴⁷Sc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹⁵³Sm, ¹⁹⁹Au, ^{99m}Tc, ¹¹¹In, ¹²⁴I, ¹⁸F, ¹¹C, ¹⁹⁸Au, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br, ¹³N, ^{34m}Cl, ³⁸Cl, ^{52m}Mn, ⁵⁵Co, ⁶²Cu, ⁶⁸Ga, ⁷²As, ⁷⁶As, ⁷²Se, ⁷³Se, and ⁷⁵Se.
 - 30. 39. (Cancelled)
 - 40. (Previously presented) The method of claim 18, wherein the subject has a cancer.
- 41. (Currently amended) A method of <u>killing a target cell in a subject</u> delivering a radiolabeled immunotoxin to a subject suspected of having a cancer, the method comprising:
 - (a) identifying a subject suspected of having a cancer; and
- (b) administering to the subject a radiolabeled immunotoxin comprising a toxic domain, a targeting domain, and at least one radionuclide atom,

wherein the targeting domain is a sFv antibody fragment that binds to a target molecule on a cancer cell in the subject, the target molecule being selected from the group consisting of Her-2/neu, a mucin molecule, CEA, PSA, folate binding receptor, A33 alpha fetoprotein, CA-125 glycoprotein, colon-specific antigen p, ferritin, p-glycoprotein, G250, OA3, PEM glycoprotein, L6 antigen, 19-9, P97, placental alkaline phosphatase, 7E11-C5, 17-1A, TAG-72, 40 kDa glycoprotein, URO-8, a tyrosinase, an interleukin- (IL-)2 receptor polypeptide, an IL-3

Serial No. : 09/910,639 Filed : July 20, 2001 Page : 5 of 12

receptor polypeptide, an IL-13 receptor polypeptide, an IL-4 receptor polypeptide, a VEGF receptor, a GM-CSF receptor polypeptide, an EGF receptor polypeptide, an insulin receptor polypeptide, an insulin-like growth factor receptor polypeptide, transferrin receptor, estrogen receptor, a T cell receptor (TCR) α-chain, a TCR β-chain, a CD4 polypeptide, a CD8 polypeptide, a CD7 polypeptide, a B cell Ig heavy chain, a B cell Ig light chain, a CD19 polypeptide, a CD20 polypeptide, a CD22 polypeptide, a MAGE polypeptide, a BAGE polypeptide, a GAGE polypeptide, a RAGE polypeptide, a PRAME polypeptide, and a GnTV polypeptide, and

wherein the at least one radionuclide atom is selected from the group consisting of 90 Y, 186 Re, 188 Re, 64 Cu, 67 Cu, 212 Pb, 212 Bi, 213 Bi, 123 I, 131 I, 211 At, 177 Lu, 47 Sc, 105 Rh, 109 Pd, 153 Sm, and 199 Au[[,]]

wherein the method is a method of killing a target cell in the subject.

- 42. (Previously presented) The method of claim 41, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α -sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).
- 43. (Previously presented) The method of claim 41, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.
- 44. (Previously presented) The method of claim 43, wherein the functional fragment comprises amino acids 1-389 of DT.
- 45. (Previously presented) The method of claim 41, wherein the cancer cell is selected from the group consisting of a neural tissue cancer cell, a melanoma cell, a breast cancer cell, a lung cancer cell, a gastrointestinal cancer cell, an ovarian cancer cell, a testicular cancer cell, a lung cancer cell, a prostate cancer cell, a cervical cancer cell, a bladder cancer cell, a vaginal

Serial No.: 09/910,639 Filed: July 20, 2001 Page: 6 of 12

cancer cell, a liver cancer cell, a renal cancer cell, a bone cancer cell, and a vascular tissue cancer

cell.

46. (Previously presented) The method of claim 41, wherein the target molecule is Her-2/neu.

47. (Cancelled)

- 48. (Currently amended) A method of delivering a radiolabeled immunotoxin to a subject suspected of having a cancer, the An imaging method comprising:
 - (a) identifying a subject suspected of having a cancer; and
- (b) administering to the subject a radiolabeled immunotoxin comprising a toxic domain, a targeting domain, and at least one radionuclide atom,

wherein the targeting domain is a sFv antibody fragment that binds to a target molecule on a cancer cell in the subject, the target molecule being selected from the group consisting of Her-2/neu, a mucin molecule, CEA, PSA, folate binding receptor, A33 alpha fetoprotein, CA-125 glycoprotein, colon-specific antigen p, ferritin, p-glycoprotein, G250, OA3, PEM glycoprotein, L6 antigen, 19-9, P97, placental alkaline phosphatase, 7E11-C5, 17-1A, TAG-72, 40 kDa glycoprotein, URO-8, a tyrosinase, an interleukin- (IL-)2 receptor polypeptide, an IL-3 receptor polypeptide, an IL-13 receptor polypeptide, an IL-4 receptor polypeptide, a VEGF receptor, a GM-CSF receptor polypeptide, an EGF receptor polypeptide, an insulin receptor polypeptide, an insulin-like growth factor receptor polypeptide, transferrin receptor, estrogen receptor, a T cell receptor (TCR) α -chain, a TCR β -chain, a CD4 polypeptide, a CD8 polypeptide, a CD7 polypeptide, a B cell Ig heavy chain, a B cell Ig light chain, a CD19 polypeptide, a GAGE polypeptide, a RAGE polypeptide, a PRAME polypeptide, and a GnTV polypeptide, and

the at least one radionuclide atom is selected from the group consisting of ¹⁸⁶Re, ¹⁸⁸Re, ⁶⁴Cu, ⁶⁷Cu, ²¹²Bi, ¹²³I, ¹³¹I, ²¹¹At, ¹⁷⁷Lu, ⁴⁷Sc, ¹⁰⁵Rh, ¹⁰⁹Pd, ¹⁵³Sm, ¹⁹⁹Au, ^{99m}Tc, ¹¹¹In, ¹²⁴I, ¹⁸F,

Serial No. : 09/910,639 Filed : July 20, 2001 Page : 7 of 12

¹¹C, ¹⁹⁸Au, ⁷⁵Br, ⁷⁶Br, ⁷⁷Br, ¹³N, ^{34m}Cl, ³⁸Cl, ^{52m}Mn, ⁵⁵Co, ⁶²Cu, ⁶⁸Ga, ⁷²As, ⁷⁶As, ⁷²Se, ⁷³Se, and ⁷⁵Se[[,]]

wherein the method is an imaging method.

- 49. (Previously presented) The method of claim 48, wherein the cancer cell is selected from the group consisting of a neural tissue cancer cell, a melanoma cell, a breast cancer cell, a lung cancer cell, a gastrointestinal cancer cell, an ovarian cancer cell, a testicular cancer cell, a lung cancer cell, a prostate cancer cell, a cervical cancer cell, a bladder cancer cell, a vaginal cancer cell, a liver cancer cell, a renal cancer cell, a bone cancer cell, and a vascular tissue cancer cell.
- 50. (Previously presented) The method of claim 48, wherein the target molecule is Her-2/neu.

51. (Cancelled)

- 52. (New) The method of claim 48, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α-sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).
- 53. (New) The method of claim 48, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.
- 54. (New) The method of claim 53, wherein the functional fragment comprises amino acids 1-389 of DT.
 - 55. (New) The method of claim 41, wherein the subject has a cancer.

Serial No. : 09/910,639 Filed : July 20, 2001 Page : 8 of 12

56. (New) The method of claim 48, wherein the subject has a cancer.

- 57. (New) The method of claim 24, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α-sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).
- 58. (New) The method of claim 24, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.
- 59. (New) The method of claim 58, wherein the functional fragment comprises amino acids 1-389 of DT.
- 60. (New) The method of claim 46, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α-sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).
- 61. (New) The method of claim 46, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.
- 62. (New) The method of claim 61, wherein the functional fragment comprises amino acids 1-389 of DT.
- 63. (New) The method of claim 50, wherein the toxic domain is a toxic polypeptide selected from the group consisting of: (a) ricin, (b) *Pseudomonas* exotoxin (PE); (c) bryodin; (d) gelonin; (e) α-sarcin; (f) aspergillin; (g) restrictocin; (h) angiogenin; (i) saporin; (j) abrin; (k) pokeweed antiviral protein (PAP); (l) a ribonuclease; (m) a pro-apoptotic polypeptide, and (n) a functional fragment of any of (a)-(m).

Serial No.: 09/910,639 Filed : July 20, 2001 Page : 9 of 12

64. (New) The method of claim 50, wherein the toxic domain is diphtheria toxin (DT) or a functional fragment thereof.

65. (New) The method of claim 64, wherein the functional fragment comprises amino acids 1-389 of DT.